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Autoimmune Hemolytic Anemia – An Interesting Case Report

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ABSTRACT

Autoimmune hemolytic anemia is one of the causes of acquired hemolytic anemia. Autoimmune hemolytic anemia (warm) occurs due to antibodies (IgG) which cross-react with the antigens present on the red blood cell (RBC) surface at body temperature. Several factors may be responsible for causing autoimmune hemolytic anemia (warm), including preceding viral infections, autoimmune and connective tissue disease, immune deficiency diseases, malignancy, prior allogeneic blood transfusion, drugs or hematopoietic cell transplantation or solid organ transplantation. Presented here is the case of a 47-year-old female who presented with severe pallor and icterus. A diagnosis of autoimmune hemolytic anemia (warm) was arrived at and the patient was treated with oral and parenteral steroids.

Keywords: Hemoglobin, direct Coombs test, autoimmune hemolytic anemia

Anemia can occur as a result of various causes, one of which is acquired hemolytic anemia. One of the causes of acquired hemolytic anemia is autoimmune hemolytic anemia, which itself has two further subtypes, i.e., warm and cold. Autoimmune hemolytic anemia (warm) occurs due to antibodies (IgG) which cross-react with the antigens present on the red blood cell (RBC) surface at body temperature. Destruction of RBC occurs at body temperature unlike cold agglutinin disease, where destruction of RBC occurs mostly at colder temperature and in cooler parts of the body. It may be associated with systemic lupus erythematosus (SLE) in about 10% of the population.

CASE REPORT

A 47-year-old female came with chief complaints of breathlessness, aggravated on exertion or activity and not improved on taking rest. There was no shortness of breath on lying flat or any attack of severe shortness of breath and coughing at night. There was no history of chest pain or abdominal pain. And no history of reduced renal output. Additionally, there was no history of altered sensorium or loss of consciousness or weight loss, no history of fever, loose stools, nausea, vomiting or drug allergy. Her bowel and bladder habits were regular, appetite reduced and reduced sleep. She was not a known case of diabetes mellitus, hypertension, tuberculosis, bronchial asthma, prior surgery or epilepsy.

Examination

On examination, patient was moderately built and nourished. She looked tired and dehydrated. She was conscious, oriented and afebrile. She had severe pallor and icterus was present. There was no cyanosis, clubbing, lymphadenopathy or edema. Cardiovascular system examination was normal with S1 and S2 heard, no murmurs were present and so was respiratory system examination with bilateral air entry present and no added sounds present. CNS examination did not reveal any significant findings, with no focal neurological deficit and per abdomen examination did not reveal any anomaly like tenderness or organomegaly. Her blood pressure was 120/80 mmHg, respiratory rate was 98 bpm. Capillary blood glucose was 102 mg/dL and her saturation were 99% at room air.

Investigations and Management

All routine investigations were sent. On account of signs of severe anemia, we sent for urgent complete blood count. Her hemoglobin turned out to be 2.8 g/dL,

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white blood cell (WBC) count was 6,050 cells/mm^3, erythrocyte sedimentation rate (ESR) was 45 mm at 1st hour, platelet count was 1.21 lakh cells/mm^3, packed cell volume (PCV) was 35.7. We immediately planned for 2 packed cell transfusion. However, we couldn't transfuse it because of cross-reaction. Meanwhile, her other investigation reports came out which showed liver functions to be mildly deranged, with serum glutamic-oxaloacetic transaminase (SGOT) of 63.1 (normal <31), serum glutamic-pyruvic transaminase (SGPT) of 41.2 (normal <34) and lactate dehydrogenase (LDH) of 811 (normal 225-450). Her renal function test parameters were normal with urea 26.7, creatinine 0.94. Her serum iron was 197 (normal 50-170). Stool occult was negative and so was C-reactive protein (CRP). Her peripheral smear showed predominantly normocytic normochromic red blood cell (RBC) with few macrocytes, occasional spherocytes and few normoblasts. Total leukocyte count was mildly increased. Platelet clumps were adequate and mildly increased. Her reticulocyte count was 31.5%. Based on the above values, the provisional diagnosis was hemolytic anemia with differential diagnosis narrowed down to autoimmune hemolytic anemia, B12 deficiency anemia and pernicious anemia.

Further investigations were ordered. Her red cell glucose-6-phosphate dehydrogenase (G6PD) enzyme screening test showed normal enzyme activity, isopropanol stability test for unstable hemoglobin was negative, direct Coombs test was positive (++) and Ham's test was negative. Bone marrow aspiration cytology showed hypercellular marrow showing severe erythroid hyperplasia with mild megaloblastic like picture. The ANA (antinuclear antibody) was positive with a value of 1.4 and anti-dsDNA was also positive with a value of 1.2. Hemoglobin electrophoresis using starch agarose gel method was normal. Serum electrophoresis report showed increase in gamma-globulin and decrease in albumin. Thus, a final diagnosis of autoimmune hemolytic anemia (warm) was made. She was treated with oral and parenteral steroids and was kept under antibiotics coverage. No packed cell transfusion was done. Her hemoglobin, which was 2.8 mg/dL at admission, gradually increased over the next few days. Day 2 hemoglobin was 2.7 mg/dL, which rose to 3.1 mg/dL at Day 3, 3.1 mg/dL at Day 4, 4.7 mg/dL at Day 5 and 5.2 mg/dL at Day 6. She was then discharged at request with a hemoglobin of 5.2 mg/dL. Thus, without even transfusing a single pint of blood, her hemoglobin was corrected with the use of steroids only.

Follow-up

She is under regular follow-up. Her hemoglobin at end of 2 months is 11.3 g/dL.

DISCUSSION

Autoimmune hemolytic anemia (warm) may occur due to various causes. It may be due to preceding viral infections, autoimmune and connective tissue disease (e.g., SLE, autoimmune lymphoproliferative syndrome), immune deficiency diseases, malignancy (Non-Hodgkin lymphoma, chronic lymphocytic leukemia [especially those being treated with purine analogues]), prior allogeneic blood transfusion, drugs or hematopoietic cell transplantation or solid organ transplantation. Clinical features depend not only on the amount but also the effectiveness of the causative antibody. Most of the patients are generally moderately to severely anemic. Symptoms also depends on the clinical severity of the disease, whether the patient is exerting or not and whether there is a presence of a concurrent illness (e.g., underlying cardiac disease). Symptoms seem to occur when the hemoglobin concentration falls below 8-9 g/dL at rest, or at a higher hemoglobin concentration during exertion. The primary symptoms include varying degrees of fatigue, dyspnea at rest, exertional dyspnea and signs and symptoms of the hyperdynamic state, such as bounding pulses, palpitations. If the hemoglobin does fall below a certain level which is required to sustain sufficient oxygenation, the patient may become confused, lethargic and dyspneic with tachycardia. Physical examination may show varying degrees of jaundice and pallor.

The findings include hemolytic anemia of varying severity, reticulocytosis in response to the anemia, the presence of spherocytic red cells on the peripheral blood smear, and a positive direct antiglobulin (Coombs) test. Serum haptoglobin levels may be reduced, serum levels of LDH will be elevated, serum levels of indirect bilirubin are also elevated, the peripheral blood smear usually shows the presence of spherocytosis. Ninety-seven to ninety-nine percent of patients with warm agglutinin autoimmune hemolytic anemia will exhibit a positive result with anti-IgG, anti-C3 or both, compared with <1% of the normal population. The Coombs test can be quantitated by an estimate of the degree of agglutination, or by more quantitative methods such as enzyme-linked immunosorbent assay (ELISA), immunoassay techniques or flow cytometry.

The workup for all patients should include the following:

- Complete blood count with RBC indices (e.g., mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC]), reticulocyte percentage, absolute reticulocyte count and examination of the peripheral blood smear.
- Tests for hemolysis, including indirect bilirubin, LDH and haptoglobin.
- Direct Coombs testing (also called direct anti-globulin test [DAT]), including testing for both IgG and C3 on the red cell surface.
- Testing for specificity of the antibody for antigens identified on RBCs.

The diagnosis of warm agglutinin autoimmune hemolytic anemia is made when all of the following are present:

- Hemolytic anemia (anemia, high LDH, low haptoglobin, high indirect bilirubin)
- Presence of spherocytic RBCs on the peripheral blood smear
- Positive direct antiglobulin (Coombs) test for the presence of IgG or C3d (after ruling out cold agglutinin disease) or both.

While in most cases, there will also be an absolute increase in reticulocytes, such reticulocytosis is a nonspecific erythropoietic response to anemia of any cause, and may not be seen initially in some patients. Differential diagnosis includes mostly paroxysmal cold hemoglobinuria and hereditary spherocytosis.

The onset of idiopathic warm or cold autoimmune hemolytic anemia may either precede or follow the diagnosis of a lymphoproliferative disorder. The following are the risk factors for development of lymphoproliferative disorder in this group of patients: advanced age, underlying autoimmune disease and the presence of a monoclonal IgM gammopathy. An increased risk for venous thromboembolism, occasionally fatal, has been described in adults with idiopathic autoimmune hemolytic anemia, especially those with concurrent HIV infection.

CONCLUSION

Our patient presented with breathlessness which was aggravated on exertion or activity and did not improve on taking rest. There was no significant medical history. She had severe pallor and icterus. Her hemoglobin was 2.8 g/dL, WBC count was 6,050 cells/mm^3, ESR was 45 mm at 1st hour, platelet count was 1.21 lakh cells/mm^3, PCV was 35.7. We immediately planned for 2 packed cell transfusion, but it could not be done because of cross-reaction.

Further tests were ordered and a final diagnosis of autoimmune hemolytic anemia (warm) was made. She was treated with oral and parenteral steroids and was kept under antibiotics coverage. No packed cell transfusion was done. This case is an excellent example of managing a patient with autoimmune hemolytic anemia without transfusing a single pint of blood. Her hemoglobin was corrected with the use of steroids only.

SUGGESTED READING

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WHO Head Points to 'Green Shoots of Hope' in COVID-19 Pandemic

While COVID-19 cases hit the 20 million mark worldwide, the chief of the WHO, Tedros Adhanom Ghebreyesus, has hinted at 'green shoots of hope'.

The WHO head has urged both governments and people across the globe to work to suppress the novel coronavirus. He stated that there are green shoots of hope and no matter where a country, a region, a city or a town is, there is still time to turn the outbreak around. He added that leaders have to step up to take action and citizens must follow the new measures… (*UN*)

29% of World's New COVID-19 Cases in India

New Delhi: India hit a new high on 9th August in its share of global COVID-19 case numbers. About 29% of all new cases and 21% of all deaths from coronavirus reported on the day were from India. India reported the largest share in the world numbers on the day in both the counts.

India's share of global cases so far this month has been the highest, with a cumulative count of 5,19,351 cases in the first 9 days of this month. The US recorded 4,93,376 cases during the same period and Brazil recorded 3,69,284 cases… (*ET Healthworld – TNN*)

FDA OKs New Opioid for Intravenous Use in Hospitals

The US FDA has granted approval to oliceridine, an opioid agonist to manage moderate-to-severe acute pain in adults, where the pain is severe enough to need an intravenous opioid and alternative treatments are inadequate.

Oliceridine is indicated for short-term intravenous use in hospitals or other controlled clinical settings, for instance, during inpatient and outpatient procedures. The drug is not indicated for at-home use. Controlled and open-label trials assessed the opioid in 1,535 patients with moderate-to-severe acute pain. It was compared to placebo in randomized, controlled studies of patients who underwent bunion surgery or abdominal surgery. Patients given oliceridine had decreased pain compared to placebo at the approved doses… (*FDA*)